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NOTICE OF ALLOWANCE AND FEE(S) DUE

26161 7590 06/16/2004  
FISH & RICHARDSON PC  
225 FRANKLIN ST  
BOSTON, MA 02110

EXAMINER

NICKOL, GARY B

ART UNIT PAPER NUMBER

1642

DATE MAILED: 06/16/2004

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,817	02/22/2002	Kornelia Polyak	00530-094001/ DFCI#689	3070

TITLE OF INVENTION: HIN-1, A TUMOR SUPPRESSOR GENE

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	YES	\$665	\$300	\$965	09/16/2004

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status.  
See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER:** Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

# **PART B - FEE(S) TRANSMITTAL**

Complete and send this form, together with applicable fee(s), to: **Mail**

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or **Fax (703) 746-4000**

**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

26161 7590 06/16/2004

**FISH & RICHARDSON PC  
225 FRANKLIN ST  
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## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

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nonprovisional	YES	\$665	\$300	\$965	09/16/2004

EXAMINER	ART UNIT	CLASS-SUBCLASS
NICKOL, GARY B	1642	435-007230

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 \_\_\_\_\_

2 \_\_\_\_\_

3 \_\_\_\_\_

## **3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)**

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent); ☐ individual ☐ corporation or other private group entity ☐ government

### **4a. The following fee(s) are enclosed:**

- ☐ Issue Fee
- ☐ Publication Fee
- ☐ Advance Order - # of Copies \_\_\_\_\_

### **4b. Payment of Fee(s):**

- ☐ A check in the amount of the fee(s) is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature)

(Date)

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Alexandria, Virginia 22313-1450. **DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Alexandria, Virginia 22313-1450.**

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TRANSMIT THIS FORM WITH FEE(S)



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10/081,817	02/22/2002	Kornelia Polyak	00530-094001/ DFCI#689	3070
26161	7590	06/16/2004	EXAMINER NICKOL, GARY B	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			ART UNIT 1642	PAPER NUMBER
DATE MAILED: 06/16/2004				

## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

**Notice of Allowability**

Application No.

10/081,817

Examiner

Gary B. Nickol Ph.D.

Applicant(s)

POLYAK ET AL.

Art Unit

1642

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 06-04-04.
2. ☒ The allowed claim(s) is/are 23,24,35 and 38-46.
3. ☐ The drawings filed on \_\_\_\_\_ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
  1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
  6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
    - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
    - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date \_\_\_\_\_
4. ☐ Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

  
**GARY NICKOL**  
**PRIMARY EXAMINER**

Gary B. Nickol Ph.D.  
Primary Examiner  
Art Unit: 1642

Art Unit: 1642

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Stuart Macphail, Ph.D., J.D. on June 4, 2004.

The application has been amended as follows:

23. (Currently amended) A method of diagnosis, the method comprising:

(a) providing a test cell;

(b) determining, in the test cell, the degree of methylation of one or more C residues in a nucleotide sequence in a genomic segment, the genomic segment ~~consisting of comprising~~ (i) a CpG island in the HIN-1 5' promoter region (SEQ ID NO:19) and (ii) the first twelve nucleotides of SEQ ID NO:3, wherein the one or more C residues are C residues in CpG sequences; and

(c) comparing the degree of methylation of the one or more C residues to the degree of methylation of corresponding one or more C residues in a corresponding genomic segment in a control cell, wherein a higher degree of methylation of the one or more C residues in the test cell than in the control cell is an indication that the test cell is a cancer cell.

24. (Original) The method of claim 23, wherein the test cell is a breast cell.

25.-34. (Cancelled)

35. (Previously presented) The method of claim 23, wherein the test cell is selected from the group consisting of a lung cell, a prostate cell, a pancreatic cell, a gastrointestinal cell, and a skin cell.

36. (Cancelled)

37. (Cancelled)

38. (Previously presented) The method of claim 23, wherein the nucleotide sequence comprises nucleotide 1 to nucleotide 252 of SEQ ID NO:19.

39. (Previously presented) The method of claim 23, wherein the nucleotide sequence consists of nucleotide 1 to nucleotide 252 of SEQ ID NO:19.

40. (Previously presented) The method of claim 23, wherein the nucleotide sequence comprises nucleotide 229 to nucleotide 551 of SEQ ID NO:19 and nucleotide 1 to nucleotide 12 of SEQ ID NO:3.

41. (Previously presented) The method of claim 23, wherein the nucleotide sequence consists of nucleotide 229 to nucleotide 551 of SEQ ID NO:19 and nucleotide 1 to nucleotide 12 of SEQ ID NO:3.

42. (Previously presented) The method of claim 23, wherein the nucleotide sequence comprises SEQ ID NO:19 and nucleotide 1 to nucleotide 12 of SEQ ID NO:3.

43. (Previously presented) The method of claim 23, wherein the nucleotide sequence consists of SEQ ID NO:19 and nucleotide 1 to nucleotide 12 of SEQ ID NO:3.

44. (Previously presented) The method of claim 23, wherein the test cell is a human cell.

45. (Previously presented) The method of claim 23, wherein the degree of methylation is determined by sequencing of bisulfite-treated DNA comprising the nucleotide sequence.

46. (Previously presented) The method of claim 23, wherein the degree of methylation is determined by a methylation-specific polymerase chain reaction (MCP) assay.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.


Art Unit: 1642

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.  
Primary Examiner  
Art Unit 1642

June 11, 2004

  
**GARY NICKOL**  
**PRIMARY EXAMINER**

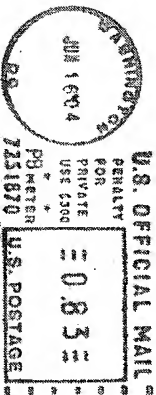
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